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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/748,739	12/26/2000	Oksana Lockridge	P-IX 4143	4261

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EXAMINER
CELSA, BENNETT M

ART UNIT	PAPER NUMBER
1639	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

file copy

Office Action Summary

Application No.	Applicant(s)
09/748,739	Lockridge et al.
Examiner	**Art Unit**
Bennett Celsa	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above, claim(s) *3-39* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1 and 2* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *3*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

Claims 1-39 are currently pending.

Claims 1-2 are under consideration to the extent they read on the elected invention.

Claims 3-39 are withdrawn from consideration as being directed to a nonelected invention.

Election/Restriction

1. Applicant's election with traverse of Group I (claims 1-2, in part, drawn to a peptide comprising substantially the same amino acid sequence as seq. Id 2) in Paper No. 10 is acknowledged. The traversal is on the ground(s) that restricting between a peptide comprising substantially sequence of a given peptide sequence AND a peptide comprising substantially the same sequence of a functional fragment of a sequence (e.g. Group I and II) is not proper since the search is not burdensome e.g. a search of group I will uncover art relevant to group II and group I and II are classified similarly, . This is not found persuasive for the reasons provided in the Restriction/Election e.g. the fragment will require different and separately burdensome, manual and computer sequence and bibliographic searches. Additionally, contrary to applicant's argument, and as discussed in the restriction/election requirement, the fragment, will be classifiable in different subclasses as compared to the entire sequence. .

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (LACK OF WRITTEN DESCRIPTION).

Claims 1 and 2, encompass peptides that are "butyrylcholinesterase variants" (e.g see specification pages 7-11; 16-17) that are"substantially the same" as seq. 2: (e.g. a peptide of 602 amino acids) which include peptide sequences identical to seq. 2 as well as any other peptide having **one or more amino** acid changes (deletions, additions, substitutions or any other alteration etc.); such alterations employing not only the 20 naturally occurring amino acids but the corresponding 20 D-amino acids as well as "amino acid analogues" and "amino acid mimetics" as long as the resulting "variant" is "substantially the same" e.g. exhibits cocaine hydrolysis activity ((increased/decreased/same) and is the same or has "a similar , nonidentical sequence that is considered by those skilled in the art to be a functionally equivalent amino acid sequence". Although the specification recites that a "variant" can have "at least 70% (or more)" sequence identity, the claims are not so limited. Accordingly, the parameters to be followed by a skilled artisan to determine "functional equivalence" are not circumscribed by either the specification or

the claims. Additionally, the term "mimetic" and "analog" is not defined by the specification and the degree of structure and/or functional properties that constitute an "amino acid mimetic(analogue)" (relative to a given standard amino acid) is not defined nor is the means and conditions of measurement. Further, the term "substantially the same amino acid sequence" is a relative term which renders the claim indefinite since this term is not precisely defined by the claim, nor does the specification provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Accordingly, the term "butyrlcholinesterase variant" is equally "relative" and indefinite. Even specifying that the "variant" possess "a 15-fold increase in hydrolysis activity" does not render claim 1 definite for the following reasons. First, the definition of "butylcholinesterase" encompasses any native mammalian butylcholinesterase and "isotype variation, polymorphism or any other allelic variation(s) " thereof . Accordingly, there is NO specific butylcholinesterase standard for measuring increased hydrolysis activity. Secondly, specifying hydrolysis activity does not address the structural lack of metes and bounds regarding the term "variant" as discussed above.

Thus, the claimed invention encompasses billions of potential deletion/substitution/addition or other alteration) variant derivable from of the 602 amino acid protein of seq. Id 2, using only the 20 natural amino acids and the 20 corresponding D-amino acids as monomers [e.g. without use of "amino acid analogs (or mimetics)]. These variants need not share any decipherable common peptide core structure.

In support of the claimed "butylcholinesterase variants" of such diverse sequence structure, the specification provides four (4) butyrcholineterase variants of identical peptide length each of which has only one variation e.g. a single natural amino acid substitution.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to a generic of compounds; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the compound or generic(s). For example, in a recent court case in line with *Eli Lilly, Judge Lourie writing for the CAFC* made the following observation:

> "A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) having the function of lessening inflammation of tissues, fails to distinguish any steroid from others having the same activity or function. Similarly, the expression "an antibiotic

penicillin" fails to distinguish a particular penicillin molecule from others possessing the same activity. "

See: J. Lourie decision in *Enzo Biochem, Inc. v. Gen-Probe Inc. et al.* No. 01-1230 (CAFC: Decided April 2, 2002) (citation forthcoming).

In this regard, applicant is referred to the seminal case of *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and the "Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, 'Written Description' Requirement" published in 1242 OG 168-178 (January 30, 2001).

It is noted that **written description is legally distinct from enablement**: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co.*

As pointed out above, the specification discloses only limited examples that are neither representative of the claimed "butyrcholinesterase variants"; nor do 4 species represent a substantial portion of the claimed genus sufficient to satisfy the description requirement

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1 and 2, the "butyrylcholinesterase variants" and "substantially the same" and their corresponding specification definitions lack particularity and metes and bounds and are thus indefinite. The term "butyrylcholinesterase variants" (e.g see specification pages 7-11; 16-17) encompass peptides that are "substantially the same" as seq. 2: (e.g. a peptide of 602 amino acids) which include peptide sequences identical to seq. 2 as well as any other peptide having **one or more amino** acid changes (deletions, additions, substitutions or any other alteration etc.); such alterations employing not only the 20 naturally occurring amino acids but the corresponding 20 D-amino acids as well as "amino acid analogues" and "amino acid mimetics" as long as the resulting "variant" is "substantially the same" e.g. exhibits cocaine hydrolysis activity ((increased/decreased/same) and is the same or has "a similar , nonidentical sequence that is considered by those skilled in the art to be a functionally equivalent amino acid sequence". Although the specification recites that a "variant" can have "at least 70% (or more)" sequence identity, the claims are not so limited. Accordingly, the parameters to be followed by a skilled artisan to determine "functional equivalence" are not circumscribed by either the specification or the claims. Additionally, the term "mimetic" and "analog" is not defined by the specification and

the degree of structure and/or functional properties that constitute an "amino acid mimetic(analogue)" (relative to a given standard amino acid) is not defined nor is the means and conditions of measurement. Further, the term "substantially the same amino acid sequence" is a relative term which renders the claim indefinite since this term is not precisely defined by the claim, nor does the specification provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Accordingly, the term "butyrlcholinesterase variant" is equally "relative" and indefinite. Even specifying that the "variant" possess "a 15-fold increase in hydrolysis activity" does not render claim 1 definite for the following reasons. First, the definition of "butylcholinesterase" encompasses any native mammalian butylcholinesterase and "isotype variation, polymorphism or any other allelic variation(s) " thereof . Accordingly, there is NO specific butylcholinesterase standard for measuring increased hydrolysis activity. Secondly, specifying hydrolysis activity does not address the structural lack of metes and bounds regarding the term "variant" as discussed above.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 1-2 are rejected under 35 U.S.C. 102(a,e,b) as being anticipated by Broomfield et al. US Pat. No. 6,001,625 (12/99).

Broomfield et al. disclose human (h) acetylcholinesterase (e.g. reference seq. Id. 1) peptide and "variants" thereof (e..g see reference seq. Id. No. 2-18) which differ by one amino acid substitution to presently claimed seq. Id 2 and thus are "substantially the same" as presently claimed seq. Id. No. 2 (e.g have greater than 99% sequence identity) ; and accordingly, anticipate present claim 1. The peptide reference structure is within the scope of the presently claimed invention, accordingly, the skilled artisan would expect properties which are derived from such a chemical structure (e.g. have a 15-fold increase in cocaine hydrolase activity) to be inherent properties of the reference peptide (s) and thus anticipate present claim 2. See MPEP

2112. The Examiner lacks the laboratory facilities to determine the physicochemical properties of a given compound.

8. Claims 1-2 are rejected under 35 U.S.C. 102(a, b) as being anticipated by Sevigny et al. WO 99/66072 (12/23/99).

Sevigny et al. disclose human (h) wild-type acetylcholinesterase (e.g. see example 1, figure 3) peptide and an allelic "variant" thereof (e.g BCHE-K which has the wild type Ala replaced with Thr at position 567; see e.g. figure 4) which differ by one amino acid substitution to presently claimed seq. Id 2 and thus are "substantially the same" as presently claimed seq. Id. No. 2 (e.g have greater than 99% sequence identity) ; and accordingly, anticipate present claim 1. The peptide reference structure is within the scope of the presently claimed invention, accordingly, the skilled artisan would expect properties which are derived from such a chemical structure (e.g. have a 15-fold increase in cocaine hydrolase activity) to be inherent properties of the reference peptide (s) and thus anticipate present claim 2. See MPEP 2112. The Examiner lacks the laboratory facilities to determine the physicochemical properties of a given compound.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-2 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of U.S. Patent No. 6,001,625. Although the conflicting claims are not identical, they are not patentably distinct from each other because patent claim 10 teaches a " variant" of disclosed human (h) acetylcholinesterase (e.g. reference seq. Id. 1) which differs by one amino acid substitution and thus which is "substantially the same" as presently claimed seq. Id. No. 2 and thus anticipate present claim 1. The peptide reference structure is within the scope of the presently claimed invention, accordingly, the skilled artisan would expect properties which are derived from such a chemical structure (e.g. have a 15-fold increase in cocaine hydrolase activity) to be inherent properties of the reference peptide and thus anticipate present claim 2. See MPEP 2112. The Examiner lacks the laboratory facilities to determine the physicochemical properties of a given compound. .

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang (art unit 1639), can be reached at (703)306-3217.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1639)
January 31, 2003

BENNETT CELSA
PRIMARY EXAMINER